

Opium and the People: The prescription psychopharmaceutical epidemic in historical context

“The need for frequent chemical vacations from intolerable selfhood and repulsive surroundings will undoubtedly remain”

Aldous Huxley, *Doors of Perception*, 1954

The modern prescription drug epidemic

Around the world people are using more and more prescription drugs, and a large proportion of these are issued for mental disorders or distress. Antidepressants like Prozac and Paxil (Seraxat), and antipsychotics like Zyprexa have been among the best-selling agents of the last few decades. The number of prescriptions issued for antidepressants in England rose by 10% a year between 1998 and 2010, and numbers are still rising (Ilyas & Moncrieff, 2012). Currently nine per cent of the United Kingdom (UK) population are taking antidepressants at any one time, slightly higher than the European average of 7.2% (Lewer et al, 2015). In the United States 11% of people over the age of 12 take antidepressants, including almost a quarter of women in their 40s and 50s (Pratt et al, 2011).

This is a trend that is occurring in other parts of the world too, with prescriptions for antidepressants now rising faster in middle income countries like Brazil and China than in the UK and United States of America (USA) (Busfield, 2010). Prescriptions for a host of other drugs from antipsychotics to pregabalin are also rising, prescribed for a plethora of new and newly expanded mental conditions, from social anxiety disorder to bipolar disorder (Ilyas & Moncrieff, 2012). Several countries are also experiencing an increase in the use and abuse of opioid painkillers, with rising prescriptions occurring in the United States, the United Kingdom, Australia and New Zealand. More people are addicted to, and die from prescribed opiates in the United States at the moment than from heroin (Lyapustina & Alexander, 2015).

Most of these drugs are prescribed and taken for long periods of time. Two thirds of people taking antidepressants in the US have been taking them for more than two years, for example (Pratt et al, 2011). Many people take sleeping pills and anti-anxiety agents on a long-term basis, especially the elderly (Hope, 2013), and drugs like antipsychotics and ‘mood stabilisers’ are usually prescribed for years at a time. So it is not just that more people are reaching out for pharmaceutical help at a time of crisis; more people are coming to depend on these drugs in their day to day lives for months, years and often for life.

Why and how have we become such a drug-dependent a society? The answer lies partly in the fact that mainstream medicine, psychiatry and the mental health disciplines do not recognise the real nature of the drugs that are prescribed to treat mental health problems. In particular, they do not recognise that drugs like antidepressants and antipsychotics are

psychoactive, or mind-altering substances. Prescription drugs with mind-altering effects are what I refer to as ‘psychopharmaceuticals.’

Psychoactive drugs

In professional circles, the term ‘psychoactive substance’ is mainly associated with recreational drugs like alcohol and cocaine. Antidepressants are simply described as drugs that are used to treat depression, or anxiety, or various other problems. Antipsychotics are described as drugs to treat schizophrenia or psychosis, or they are referred to ‘mood stabilisers’ which are meant to treat ‘bipolar disorder’.

A psychoactive substance can be defined as a chemical that produces an altered mental state and associated changes in behaviour due to its effects on the central nervous system. Although we are most familiar with the psychoactive effects of recreational drugs like alcohol, drugs prescribed to treat mental disorders, including drugs classified as antidepressants, antipsychotics, anxiolytics, stimulants and drugs such as lithium and anticonvulsants used to treat bipolar disorder, also modify normal mental processes and behaviour. These alterations are independent of any effects they may or may not have on hypothetical underlying abnormalities or disease processes.

Just like the various substances that are used recreationally, each prescribed psychoactive drug or psychopharmaceutical, produces a distinctive altered mental and physical state, whose characteristics depend on the pharmacological properties of the particular drug. Some prescribed drugs such as stimulants (including amphetamine and methylphenidate, otherwise known as Ritalin) and benzodiazepines (including diazepam, brand name Valium, temezepam and lorazepam, brand name Ativan) produce pleasurable effects, and, for this reason, licitly and illicitly obtained supplies may be used recreationally and excessively. Others are experienced as unpleasant. This is most notably the case with the neuroleptic or antipsychotic drugs like chlorpromazine (brand names Thorazine or Largactil), haloperidol (Haldol), olanzapine (Zyprexa) and quetiapine (Seroquel), but tricyclic antidepressants and lithium are also generally disliked by volunteers (Dumont et al., 2005; Judd et al., 1977a). Selective serotonin reuptake inhibitors (SSRIs) like fluoxetine (Prozac) and paroxetine (Seroxat or Paxil) generally have weaker psychoactive effects, but the effects are found to be unpleasant when noticed (Dumont et al, 2005). The fact that these drugs are not associated with euphoria, and therefore do not usually induce craving or become drugs of abuse, does not make them any less ‘psychoactive’ than recreational drugs, nor does it exclude them from inducing physical dependence.

Table 1 summarises scientific literature and user descriptions of the principle drug-induced mental alterations associated with the major classes of drugs prescribed for mental disorders during use of the drug. Each type of drug also produces characteristic withdrawal effects after it has been stopped. It is important to remember, however, that within each so-called class of drugs there are different types of agent, with varied and distinctive pharmacological profiles and that agents between and across classes differ in the strength of their effects.

Nevertheless, a property that is common to many mind-altering drugs is a flattening out of emotional experience. Opiates, neuroleptics and SSRIs, for example, in different ways render emotions less intense, and create a state of emotional disinterest or detachment. This is in contrast to drugs like alcohol and benzodiazepines which can intensify emotions during intoxication. Regardless of their differing impact on emotions, however, all psychoactive substances impair higher brain functions to a greater or lesser extent, as American

psychiatrist, Peter Breggin, points out (Breggin, 2008). Mind-altering drugs reduce our sensitivity to our surroundings, especially to subtle environmental cues, such as the behaviour of other people. They diminish our ability to react creatively, to take initiative and think laterally. They make us less aware of other people's emotions, and less able to engage with their concerns. Of course this depends on the strength of the drug. A small dose of caffeine or nicotine makes little difference, but being under the influence of alcohol, as we know, can seriously impair a person's judgement about their situation. Moreover, we are often unaware of this impairment while we are under the influence of a mind-altering drug, a phenomenon that Breggin refers to as the 'spell-binding' effects of drugs (Breggin, 2008). It is only after we have stopped the drug, and its effects on the body have completely worn off, that we are able to properly assess how it affected us.

Drugs that produce euphoria are generally acknowledged to have psychoactive effects, at least after patents expire and profits fall. This is often associated with concern about over-use, and prescribing of benzodiazepines is now discouraged in many countries, for example. However, the disease-centred idea can obscure these effects for as long as commercial or professional incentives exist. Thus although the pleasurable and energising effects of amphetamine are well-recognised, they are rarely mentioned in the context of treating attention deficit hyperactivity disorder (ADHD), for example, as this is an area of growing professional interest and many treatments are still on patent. Pregabalin, a drug introduced into Europe in 2004 and marketed for the treatment of pain and anxiety, has been a controlled substance in the United States since 2004. In the United Kingdom, prescriptions have soared over the last 10 years, and it has become one of the most costly drugs prescribed in the National Health Service (Prescribing and Medicines Team, 2015). Warnings about its potential for misuse were only issued in December 2014 in England, however, and its use still does not attract the opprobrium attached to the prescription of opiates or benzodiazepines for the same situations (Public Health England, 2014).

Author Richard DeGrandpre suggests that psychoactive drugs are currently divided into socially sanctioned and socially disreputable substances: 'angels and demons' (see Table 2) (DeGrandpre, 2006). The angels are those drugs that are considered to be specific treatments for underlying medical conditions, and whose use is endorsed and promoted. The 'demons' are drugs that are used primarily for their mind-altering properties, whose use is either illegal or disparaged. Alcohol, as western society's principle recreational drug, is tolerated, if not actively promoted. The division is fluid, however. Benzodiazepines were first represented as specific anti-anxiety agents, but as their pleasurable effects and addictive potential became clear, they were relegated to the status of 'demons'. Amphetamine, whose use as a prescription drug declined dramatically in the 1970s following the imposition of tighter controls, is enjoying a revival of its reputation as a specific treatment for adult ADHD.

The category a drug falls into is not determined by reliable evidence of the effectiveness of drugs as treatments for underlying diseases or abnormalities, nor by the level of harm they can induce. Despite the ubiquity of the myth of the chemical imbalance, it has never been demonstrated that drugs work by targeting abnormal physiological or biochemical processes (Moncrieff, 2008a). There is, moreover, no evidence that there are specific biochemical imbalances associated with the particular mental disorders we currently identify and

diagnose. Evidence never concurred with the serotonin hypothesis of depression - it was a figment of the pharmaceutical industry's marketing departments (Lacasse & Leo, 2005; Moncrieff, 2014). The dopamine theory of schizophrenia is also at odds with most of research results, and the non-specific role of dopamine in arousal and stress, as well as uncontrolled effects of prior antipsychotic drug treatment, are likely to account for the few positive findings (Moncrieff, 2009).

Consequences of the psychopharmaceutical epidemic

Has the epidemic use of psychoactive drugs on prescription made us happier and healthier? Are we a more stable and productive society as a consequence of all the antidepressants we are consuming? Does the use of these mind-altering chemicals enable people to live more contented and fulfilling lives?

Although some of these drugs may be useful for some individuals in some situations, there is no evidence that the sort of mass prescribing that exists at present has tangible benefits for most individuals or society.

The evidence on which the use of these drugs is based consists of randomised controlled trials, in which an active drug is compared with a placebo. Outcomes are judged by comparing scores on specially devised rating scales, which are supposed to measure the symptoms of the disorder in question. None of these scales has ever been shown to really capture the problem it is meant to measure (if indeed that is possible), and the differences between the drug and the placebo are usually quite modest. In trials of antidepressants for example, meta-analyses find that the difference in scores on the commonly used Hamilton Rating Scale for Depression are less than 2 points, where the maximum score is 54 (Kirsch et al, 2002). This difference is much smaller than the difference that clinicians identify as indicating even modest improvement (as measured by the Clinical Global Impressions scale). In fact, clinicians do not notice any difference at all at differences on the Hamilton scale of 3 points or less (Moncrieff & Kirsch, 2015).

Few studies have looked at objective measures of the outcome of drug treatment, and where they have done so, the evidence suggests that drug treatment may be harmful to many people's prospects of recovery. Studies of working people with depression have found, for example, that people who take antidepressants have more time off work than those who do not (Dewa et al, 2003). Some of the difference is likely to be attributable to the fact that people with more severe disorders are more likely to be offered and accept drug treatment, but nevertheless, the findings do not provide any support for the idea that antidepressant treatment improves work performance. The correlation between rising antidepressant use and disability claims for depression and anxiety, particularly when claims for other medical conditions are falling, provides further evidence that mass antidepressant use does not improve the mental health of the population, and may make it worse (Figure 1).

Antipsychotic drugs, with their neuro-suppressant effects, reduce acute psychotic symptoms and distress, but, although long-term drug treatment is well-established and recommended practice for people with disorders like schizophrenia, the ultimate benefits of this remain uncertain. Most studies of long-term treatment have focused on measuring the risk of having a 'relapse' of the underlying condition, and few have looked at social functioning, independence or quality of life. Moreover, few studies have followed people up for more than one or two years. A non-randomised follow-up study suggested that people who took continuous medication might have a worse outcome than those who did not, but the difference between people who used drugs continuously and those who did not may be explained by differences in the severity of the underlying problem (Harrow et al, 2012).

However, a long-term follow-up of participants from a randomised controlled trial supports the idea that taking antipsychotic medication continuously for long periods may lower your chances of making a good recovery. The study consisted of a comparison between antipsychotic maintenance treatment for people with a first episode of psychosis, with a gradual and supported programme of antipsychotic reduction and discontinuation. Seven years after the programme begun, people in the group randomised to the antipsychotic discontinuation programme were over twice as likely to show a full social recovery as people allocated to maintenance treatment (Wunderink et al, 2013). Relapses, which were initially higher in the antipsychotic discontinuation group, evened out over the 7-year follow-up. Only 20% of participants in the antipsychotic discontinuation group stopped their medication completely and remained off it, with many more stopping and going back on to medication, or never completely stopping at all. Conversely, some people in the maintenance group successfully reduced or stopped their medication. Nevertheless, overall the group that was originally randomised to the supported antipsychotic reduction strategy was more likely to have stopped their medication or be taking very low doses by the time of follow-up. The study appears to suggest that even with psychotic disorders, the standard practice of taking medication for years on end reduces people's chances of making a meaningful recovery.

The benefits of long-term use of benzodiazepines, ADHD treatments and drugs prescribed for bipolar disorder have also not been established (Moncrieff, 2008a).

None of these types of drug is innocuous. Antipsychotics have well-known and potentially devastating adverse effects, including the sometimes irreversible neurological condition known as tardive dyskinesia, weight gain, diabetes, sexual dysfunction and cardiac toxicity leading to an increased risk of sudden cardiac death (Salvo et al, 2016). Antidepressants such as the SSRIs are less debilitating overall, but can also cause apathy, sexual dysfunction and a state of agitation that has been associated with increased suicidal ideation and behaviour in young people in particular (Safer & Zito, 2006). Although there is little official data, patients reports consistently indicate that stopping the drugs can lead to unpleasant and sometimes incapacitating withdrawal symptoms, which can occasionally persist for months and even for years (Fava et al, 2015).

There is little evidence, therefore, that the widespread use of psychopharmaceuticals has any objective benefits, and plenty of reasons to be concerned about their effects. Hence,

explanations for their popularity must lie outside the scientific arena. Looking at the history of humankind's relationship with mind-altering substances of all sorts helps to put the current situation in context, and points to some universal drivers of this activity.

History of psychoactive drug use

Psychoactive drugs have been a part of life in most societies and communities throughout history. They have been used for pleasure, to dull physical and emotional pain, to increase concentration and endurance and to induce states of religious ecstasy (DeGrandpre, 2006). Up until the late 19th century, there were no restrictions on the sale and availability of any sort of substance (except for price) and you could buy opium and cocaine-containing preparations from the corner shop, along with your groceries.

For centuries prior to our own time, medicinal and 'recreational' use of psychoactive substances was not clearly differentiated. In a world where medical fees were beyond the means of most ordinary people, long before the formation of the NHS and other socialised forms of health care, people treated themselves as far as they could, using the drugs that were available to them. The intoxication produced by alcohol, for example, was used for its anaesthetic effects, as well as for pleasure. Opiates (opium, morphine and heroin), which effectively deaden physical pain and emotional anguish, were widely used to dull the physical and emotional strains of the labouring classes during the industrial revolution. Many substances were sold as 'tonics' which were advertised as promoting both physical health and mental wellbeing.

The use of psychoactive substances only came to be viewed as a social problem under particular social and economic conditions. In the medieval world, the peasants could get as drunk as they liked, and no one suffered much but themselves. When wage labour and factory labour became the norm, it suddenly mattered if labourers were intoxicated and less productive than they might be. Life in emerging industrial Britain was also more than conducive to heavy drinking and drug use. Dislocated from home and family, working 12 hours a day (or more) for seven days a week, alcohol and drugs provided the worker with a quick and easily accessible escape, maybe the only one he or she could hope for.

The controls that were placed on the use of mind altering substances from the beginning of the 20th century could not stamp it out, however. Prohibition of alcohol in the United States was a resounding failure, and although the availability of opium was restricted, the pharmaceutical industry started to produce a new array of mind-altering chemicals. As options for self-prescribing became more limited, the use of mind-altering drugs came increasingly under the control of medical practitioners. Women in particular, less inclined to drown their sorrows in drink than men, started to go to the doctor to obtain a chemical salve for difficult and unfulfilling lives. As medical practitioners started to control the availability of such substances, the problems for which these drugs were used were transformed into medical problems. As this occurred the nature of the drugs and their mind-altering properties became obscure, and the reasons why people were using them were concealed beneath a medical mythology.

The problematisation of drug use

In medieval and Tudor England, heavy drinking was an accepted part of rural life. Weak beer was consumed instead of water by all the family on a daily basis, but festivals and holidays, of which there were many, were occasions for drinking to inebriation. Drunkenness was not regarded as problematic in pre-industrial society, and the country people were left to drink as they pleased.

It was in the 18th century, when the increasing urban population took to drinking gin in large quantities, that concern about alcohol use emerged. Hogarth's famous engraving, *Gin Lane*, indicates the moral outrage that had started to form around the drinking habits of the poor.

Freed from the customs and obligations of rural life and displaced into the exploitative environment of early capitalist cities, the nascent working class turned to the instant oblivion provided by the newly imported, super-strength liquor, gin. Gin was blamed for rocketing rates of crime, prostitution and debt, and the upper classes lived in fear of a breakdown of law and order, as well as bemoaning the decline in the nation's productivity. The Gin Acts of the 18th century were the first legislative attempts to control the people's use of mind-altering chemicals (Gately, 2008).

A similar same story played out with opium, which was widely used by all classes during the 19th century. The medicinal and recreational qualities of opiate drugs are particularly difficult to disentangle, and addiction to opium was likely common among working people who used it either to alleviate the pain of physical ailments, to relieve emotional strain or for enjoyment. Cocaine in various preparations was also widely available and vigorously promoted in the 19th century. Vin Mariani, a popular patent medicine developed in 1863, was one of a number of cocaine containing preparations on the market in Europe and the United States. It was made from a mixture of Bordeaux wine and coca leaves, the ethanol in the wine extracting the cocaine from the coca leaves. It was endorsed by Pope Leo XIII, who awarded it a Vatican gold medal, and appeared on advertisements which claimed the drink restored 'health, energy, strength and vitality' (Wikipedia, 2015). The performance enhancing properties of cocaine were widely recognised, and used to promote another cocaine-containing preparation, Coca-Cola.

Through the course of the 19th century concerns mounted about working class opium use. The accidental poisoning of children with opium or laudanum (a combination of opium and alcohol) fuelled public health campaigns against the drug in Britain (Berridge, 1977). These coincided with rising opposition to the British opium trade with China. The United States banned the importation of opium for smoking from 1909 with the passing of the Opium Exclusion Act and in 1912 the first of a series of international treaties obliged signatories to restrict importation of opium to medicinal preparations. In the United Kingdom drugs were blamed for the dissipation of soldiers during the first world war, and use of opium, cocaine and marijuana was made illegal by the Defence of the Realm Act 1916, which was later extended into peacetime as the Dangerous Drugs Act, 1920 (Berridge, 1977; Cockburn & St Claire, 1998).

The puritanical movement against the use of mind-altering substances culminated in national prohibition of the liquor trade in the United States, which came into effect in 1920 and lasted 13 years. Prohibition is widely acknowledged as a piece of class legislation, stimulated by concerns over working class drinking habits. It was the result of a concerted campaign by the Anti-Saloon League and its aims were never to abolish the consumption of alcohol entirely, but to shut down the saloon. Possession and consumption of alcohol were not prohibited, only its commercial trade, and those with the foresight and the resources were free to drink alcohol they had stored before prohibition came into force. When the Great Depression hit, and the masses needed pacifying, prohibition was finally repealed (Burnham, 1968).

Psychoactive drug use in the 20th century

As avenues for self-initiated use of psychoactive substances closed down, the medical profession and the pharmaceutical industry stepped into the breach. Small-scale chemists and pharmaceutical companies started to increase the scale of their development activities, production and marketing in the early 20th century, transforming into the large-scale modern industry we recognise today (Liebenau, 1987).

Barbiturate drugs first became available in 1903, and although they revolutionised anaesthesia and the treatment of epilepsy, they were most widely prescribed for anxiety and insomnia. Amphetamines, available as tablets from 1937, were prescribed for the treatment of mild depression or 'neurosis'. They were issued to pilots during world war II, and soon started to be used as diet pills (Rasmussen, 2006).

In the mid 20th century use of prescription stimulants and sedatives was rife. In 1955, the quantity of barbiturates being used in the USA was sufficient for the treatment of 10 million people on a continuous basis for a whole year, representing 6% of the population of the time, or 8.6% of the adult population (Glatt, 1962). Miltown, a barbiturate-like drug launched in the United States in 1955, was one of the first individual block-buster drugs. At the height of its popularity, apparently, demand for the drug was so high that pharmacies frequently ran out of supplies, hanging signs on their doors saying 'Out of Miltown', 'More Miltown tomorrow' (cited in Metzler, 2003). It was marketed for everything and everyone. Advertisements recommend it for 'the tense nervous patient,' 'the agitated senile patient,' 'the problem child,' 'the alcoholic' (Wallace Laboratories, 1964) and suggest that with the use of Miltown, 'pregnancy can be made a happier experience' (Wallace Laboratories, undated).

By the 1960s, amphetamines and other stimulants (e.g. Ritalin) were also in high demand. In the UK, a survey conducted in 1960 found that the quantities of amphetamine being prescribed were enough to supply 1% of the whole population with twice daily doses on a long-term basis. Eighty five per cent of prescriptions were issued to women, mostly those between the ages of 36 and 45. A third of prescriptions were issued for weight loss, a third for depression or anxiety and a third for a medley of vague complaints including tiredness, pain and psychosomatic complaints (Kiloh & Branden, 1962). By 1971, 5% of the total US population were being prescribed amphetamines (Rasmussen, 2008).

Benzodiazepines were introduced in the early 1960s, and soon became popular as a safer alternative to barbiturates (they are less dangerous in overdose than the highly toxic barbiturates). By the 1970s, benzodiazepines were being used regularly by 8% of the UK population, with 14% using them at least once a year (Balter et al, 1974). Again they were prescribed for a wide range of vague complaints including 'nerves' and unexplained physical symptoms (Lader 1978).

Drug advertising

The massive advertising campaigns that promoted these drugs played on the psychological insecurities of their age, and were mostly targeted at women. Advertisements for amphetamine paraded images of stylish, well-dressed women, suggesting the state that women should aspire to. 'Stay fit and slim' calls a 1940 advertisement, featuring the picture of an attractive young woman (Amphetamine advertisement, 1940). Ritalin 'helps relieve chronic fatigue and apathy quickly,' claims another, featuring a picture of a tired looking woman with a vacuum cleaner, who will presumably soon be vigorously vacuuming her house with the help of Ritalin's ability to restore 'alertness, enthusiasm and drive' (Ciba, 1970).

Barbiturates, Miltown and the benzodiazepines were promoted as alleviating the burdens of the post-war housewife. A 1960s advertisement for Miltown announces its usefulness for 'battered parent syndrome,' for women who are 'physically and emotionally over-worked, over-wrought and ...overwhelmed' (Wallace Laboratories, 1967). Tranquilisers, as they became known, were a means of managing the cultural anxieties of a world in which gender roles were changing dramatically (Metzl, 2003). During the second world war, women had joined the workforce and played a full role in public life, but in the 1950s, they were increasingly encouraged to retreat to the private sphere. The contradictions and frustrations of this situation were transformed into the pathology of individual women. The advertisement for 'battered parent syndrome' goes on:

'What went wrong. Is parenthood something other than the rosy fulfilment pictured by the women's magazines? Is anxiety and tension fast becoming the occupational disease of the homemaker?

Some say it is unrealistic to educate a woman and then expect her to be content with the Cub Scouts as an intellectual outlet.

Or to grant that she is socially, politically and culturally equal, while continuing to demand domestic and biological subservience.

Or to expect her to shoulder the guilt-burden of this child-centred age without unravelling around the emotional edges.

Or to compete with her husband's job for his time and involvement.

But whatever the causes, the consequences- anxiety, tension, insomnia, functional disorders- fill waiting rooms. Sometimes it helps to add Miltown to her treatment- to help her relax both

emotional and muscular tension. It's no substitute for a week in Bermuda, or for emotional readjustment. But it will often make the latter easier for her, as well as for the physician' (Wallace Laboratories, 1967).

Advertisements for benzodiazepines continued the themes of frustration and inadequacy. Some persuaded doctors that unmarried women or men, or men dominated by women, were good candidates for Valium. An advertisement for the benzodiazepine oxepam, featuring a young woman surrounded by brushes and cleaning equipment, suggests to the doctor that 'you can't set her free, but you can make her less anxious' (Wyeth Laboratories, 1967).

Feminist writer, Betty Friedan, coined the term the "Problem That Has No Name" for this mid-20th century female angst in her famous book, *The Female Mystique*:

"The problem lay buried, unspoken, for many years in the minds of American women. It was a strange stirring, a sense of dissatisfaction, a yearning [that is, a longing] that women suffered in the middle of the 20th century in the United States. Each suburban [house]wife struggled with it alone. As she made the beds, shopped for groceries ... she was afraid to ask even of herself the silent question — 'Is this all?'" (Friedan, 1963, P 15)

Rock band, *The Rolling Stones*, also captured the idea of prescription drugs as the panacea for the stifled housewife in their famous song *Mother's Little Helper*, purportedly written about Valium.

The recreational drug scene

From the 1950s onwards, the prescription of mind-altering drugs for mental health problems was paralleled by the rise of the recreational drug scene. Initially the drugs consumed recreationally were mostly diverted from medical sources. Amphetamine, barbiturates, and the famous mixture of the two, Drinamyl (purple hearts), were the party drugs of the 1950s, 60s and 70s. As late as the 1970s, the majority of illicitly consumed substances were of pharmaceutical origin. In 1972, 80-90% of the stimulants sold on the street in the US were products of pharmaceutical firms (Graham, 1972). Imported cannabis, cocaine and heroin were also widely used for recreational purposes, and after stricter controls were placed on the manufacture of amphetamine, the drug started to be manufactured illicitly in large quantities. Nevertheless, the origins of the recreational drug scene lie in the diversion of drugs prescribed by medical practitioners. The mass prescription of mind-altering drugs also helped to establish the appeal of changing one's mental state. In 1970, US senator Thomas Dodd complained that it was the pharmaceutical industry's 'multihundred million dollar advertising budgets, frequently the most costly ingredient in the price of a pill, have pill by pill, led, coaxed and seduced post world war 2 generations into the "freaked out" drug culture plaguing the nation' (Graham, 1972).

As drug use became increasingly associated with pleasure and expanding consciousness, rather than relieving distress, it became a symbol of rebellion. By the late 1960s, illicit drug use was strongly associated with the counter-culture- the hippy movement, the anti-Vietnam war protests, the 1968 student uprisings etc. Drug use was part of the revolution against conservative mores and culture and against the regimented system of capitalist production and its associated war machine. Later in the 1970s and 80s, illicit drug use, particularly of heroin and later crack cocaine, was associated with the urban underclass created by the worldwide recession, and the neoliberal economic policies enacted by Thatcher, Reagan and other world leaders.

In the early 1970s legislation was passed in the US and UK that attempted to put the genie back in the bottle. Amphetamines, along with other drugs like LSD and cannabis, became prohibited substances. Legitimate medical uses of amphetamines were restricted to narcolepsy and ADHD, production quotas were applied and prescriptions and diversion plummeted. Use of illicitly manufactured substances or imported drugs like heroin and cocaine rose to fill the gap (Rasmussen, 2008). Meanwhile prescriptions for benzodiazepines, not yet identified as ‘demons,’ continued to rise (Lader, 1991).

The professional reaction

The emerging drug scene presented a challenge to psychiatrists, whose drugs consisted entirely of psychoactive substances. To preserve the specialist aura of prescribing, and to avoid being seen as drug peddlers, the profession needed to distance itself from recreational drug use and present its practice as commensurate with the increasingly sophisticated use of drugs in other parts of medicine.

Up to and including the 1950s, the drugs administered to people with mental health problems, were understood to work through the characteristic mental and physical alterations they produced, in what I have called a ‘drug-centred’ model of drug action (Moncrieff, 2008a). The sedatives administered to the most turbulent psychotic patients were regarded as chemical restraints that had no effect on the underlying problem. The stimulants prescribed for the depressed housewife were marketed as ‘pep’ pills, much as cocaine had been advertised a century earlier. After the 1950s, however, a new understanding of drug treatment developed; the ‘disease-centred’ model of drug action. This new model, which persists to the present-day, portrays drug treatments as working by rectifying a putative underlying chemical or physiological abnormality in the brain. This alleged abnormality, or disease, is assumed to produce the mental and behavioural symptoms of a particular disorder. Hence drug treatments, according to this model, target the hypothetical biological origins of the symptoms of mental disorders.

In the 1950s, while the drug-centred model still predominated, psychiatrists took an interest in the nature of the mental and behavioural alterations their drugs produced. They provided detailed descriptions of the effects that early antipsychotics like chlorpromazine had on patients and volunteers, including their junior colleagues (Moncrieff, 2013). They compared

and contrasted the drug-induced states produced by chlorpromazine and barbiturates. Similarly, the stimulant-like properties of early antidepressants were clearly documented in contemporary accounts (Crane, 1956). Over the course of the next two decades these observations drop out of the literature, and there is an increasing silence as to the psychoactive nature of drugs used in psychiatry. By the 1990s, it ceases to occur to anyone that understanding the alterations produced by the new SSRI antidepressants or the atypical antipsychotics is important, even despite the fact that they were both promoted as having fewer adverse effects and being more 'tolerable' than their predecessors.

The 'disease-centred' model emerged alongside the illicit drug scene and enabled psychiatrists to present their treatments as specific, illness-targeting treatments, just like the drugs that were used in general medicine. By presenting psychiatric drugs as targeting underlying abnormalities, the disease-centred model helped to repackage the use of psychoactive substances as a bona fide medical treatment, quite distinct from the use of drugs in other contexts.

From the 1960s it became particularly important to distinguish newly introduced psychiatric drugs from amphetamines, since the ubiquitous use of the latter was causing increasing concern. The stimulant effects of early 'antidepressant' drugs started to be played down (Moncrieff, 2008b). Discussants at a conference held in 1962 were keen to stress how the new 'antidepressants' were 'much more specific' than stimulants (Goldman, 1966). The concept of an 'antidepressant' helped cement the medicalisation of psychoactive drug use by defining the new drugs by their proposed effects on the presumed biological mechanism of depression, rather than their pharmacological properties.

The disease-centred model was undermined, however, by the continued prolific use of benzodiazepines. By the 1980s it was clear that however much they might be trumpeted as a specific treatment for anxiety, they were being used for their tranquilising properties, prescribed to many people, especially women, in order to numb the difficulties of daily life. Moreover, despite official guidelines stating that 'the true addictive potential of benzodiazepines is low' (Committee on the Review of Medicines, 1980), evidence was accumulating to indicate that benzodiazepines were just as addictive as barbiturates or opiates. Estimates suggested a quarter of a million people might have become unknowingly addicted to medically prescribed benzodiazepines in the UK alone by the 1980s (BBC, 1983, cited in Gabe & Bury, 1991). What came to be seen as the 'tranquilliser problem' was widely covered in the media, with high profile programmes such as *That's Life* and *Brass Tacks* dedicating several episodes to the issue (Gabe & Bury, 1991).

On top of the medical addicts, short-acting benzodiazepines like temezepam rapidly became popular among problem drug users, especially people who used or were addicted to opiates. It became clear that withdrawal from benzodiazepines was just as difficult, and physically more hazardous, than withdrawal from heroin. Benzodiazepine dependence became one of the most common indications for admission to drug detoxification and rehabilitation services by the 1990s.

The chemical imbalance

The scandal over dependence and over-prescribing that erupted in the late 1980s forced the pharmaceutical industry to commit itself wholeheartedly to the disease-centred model for marketing its new drugs. Formerly, drugs were marketed in various ways. Some advertisements presented drugs like antipsychotics as disease-specific treatments, but others continued to emphasise the tranquilising properties of drugs like the benzodiazepines. In contrast, the 1990s blockbuster ‘antidepressants’ such as Prozac and Paxil were advertised not for their mind-altering qualities, but for their ability to reverse an underlying chemical imbalance. In this situation it became as important to market the disease as the drug, and companies funded ‘disease awareness’ campaigns to encourage people to think of themselves as ‘depressed’ (Breggin & Breggin, 1995).

The chemical imbalance has since become the ubiquitous justification for the prescription of mind-altering substances. Despite the fact that it has long been accepted as false, or at least unproven, the idea continues to be cited as the basis for the action of drugs in depression, bipolar disorder and adult ADHD on company websites and advertisements. Pharmaceutical marketing has been extremely effective in creating a new reality, bearing witness to Mary Boyle’s suggestion that if you say something enough times, it will become accepted as truth (Boyle, 2002). The message has been so successfully diffused throughout society that most members of the general public have been convinced that chemical abnormalities have been established in depression and that these abnormalities are corrected by antidepressants. An audience of university lecturers and professors whom I spoke to recently were quite astounded to find out that this is not, in fact, the case.

The language may have changed, but the motives remain the same. The target market has changed little too. Users of the new prescription drugs are still predominantly middle aged women, although increasing numbers of younger people and men have joined them (Lewer et al, 2015). In many countries, even treatments for adult ADHD are predominantly prescribed to women (Simon et al, 2009). In view of the fact that boys outnumber girls in childhood diagnoses by 3 to1, and adult ADHD is supposed to be a continuation of the childhood condition, this is a curious pattern. It suggests that far from treating a specific condition, drugs prescribed for ADHD, along with antidepressants, new anti-anxiety agents and treatments for bipolar disorder, are finding their way into that longstanding niche for the treatment of manufactured female inadequacy and discontent. Advertisements still feature pictures of the anxious-looking women they are trying to appeal to (Edwards, 2010), and others parade images of domestic female contentment, represented by happy-looking women with children or women serving food to their male partners (Eli Lilly, 2016).

The pros and cons of transcendence

Attitudes to the use of mind-altering drugs have changed profoundly over the last half century. First the recreational drug scene arrived, in which the use of mind-altering drugs became a subversive and rebellious activity. Second, the benzodiazepine crisis revealed the

extent to which medically prescribed substances were also being used to transport people away from a mundane or depressing reality. By the 1980s, the mass drugging of poor and unhappy women was no longer socially acceptable.

Since that time, the new versions of opium and Valium come packaged not with the idea of temporary transcendence, but with the idea that the user is biochemically flawed, and in need of a chemical fix. We are inherently defective, and our destiny and salvation is in the form of a pill.

This idea enables the mass drugging of the population to continue, and indeed to expand. It is this idea that enables powerful psychoactive drugs to be used as a treatment for troublesome behaviour in children, for example, which would otherwise no longer be acceptable. The idea that drugs are specific and targeted treatments for underlying disorders such as ADHD, depression or bipolar disorder provides the justification for the epidemic use of stimulants, antidepressants and antipsychotics in children that is sweeping the United States and creeping into Europe (Boseley, 2015).

The pharmaceutical industry knows that what constitutes a medical indication for psychoactive drug use is infinitely malleable, and that this malleability can be used to capitalise on the ancient human desire to alter one's mental state. Large swathes of the population can be persuaded to view themselves as needing drug treatment for anxiety, depression, bipolar or whatever is the flavour of the decade (Healy, 2004). Just as governments of the mid 20th century tolerated the widespread use of barbiturates and amphetamines, governments of the 21st century have shown no concern about the rapidly rising use of antidepressants, antipsychotics and medically prescribed stimulants. Although packaged as sophisticated disease-targeting interventions, they fulfil the same role that the widespread use of opium and cocaine-containing 'tinctures' did in the 19th century. They provide the promise of a quick fix, and a mind-altering experience that temporarily removes the user from unwelcome thoughts and circumstances.

The impulse for chemical transcendence is a deeply ingrained and long-standing human impulse, and one that is not necessarily harmful. When it is presented as something else, however, the natural controls that most human beings can exercise over this impulse may be over-ridden. If we are told by a doctor that a drug will simply restore us to some imagined state of biochemical normality, its spell-binding effects will be reinforced by a lack of awareness of the nature of what we are taking. Our instincts that chemical oblivion should be restricted to a few hours, and that being permanently under the influence of mind-altering substances is not a good idea, will be suppressed. We are not likely to identify or monitor how the substance changes our ordinary thinking and behaviour, and our interactions with the world around us.

The idea that we are chemically flawed is superficially attractive, but profoundly disempowering. In the short-term it may provide comfort by locating the source of unwanted feelings and responsibility for failure in our biology, but it also suggests that improvements and solutions are beyond our capability. Only with expert medical intervention and lifelong

dependence on chemicals is it possible to ameliorate the disabling defects of a faulty brain. People who are fed this message are left in a highly vulnerable state. Once started on medication, many become terrified of ever coming off it, and never have the opportunity to develop confidence in their own abilities to manage difficult situations and emotions.

Only if we unmask psychopharmaceuticals, can we start to develop a more sensible relationship with them. Using drugs to alleviate emotional pain is not wrong, but it is fraught with difficulties. As well as the bodily aberrations they produce, drugs which affect brain functioning change the way we think and behave and relate to the world. Moreover, these changes are often difficult to appreciate while under the drug's influence. In order to understand and minimise the potential damage that drugs can wreak, and to harness their effects for the good they can sometimes achieve, we need to explode the myth that the drugs prescribed for mental disorders work by correcting an underlying abnormality. We need to recognise the real nature and purpose of these drugs, and acknowledge their lineage within the many 'opiums' of previous eras.

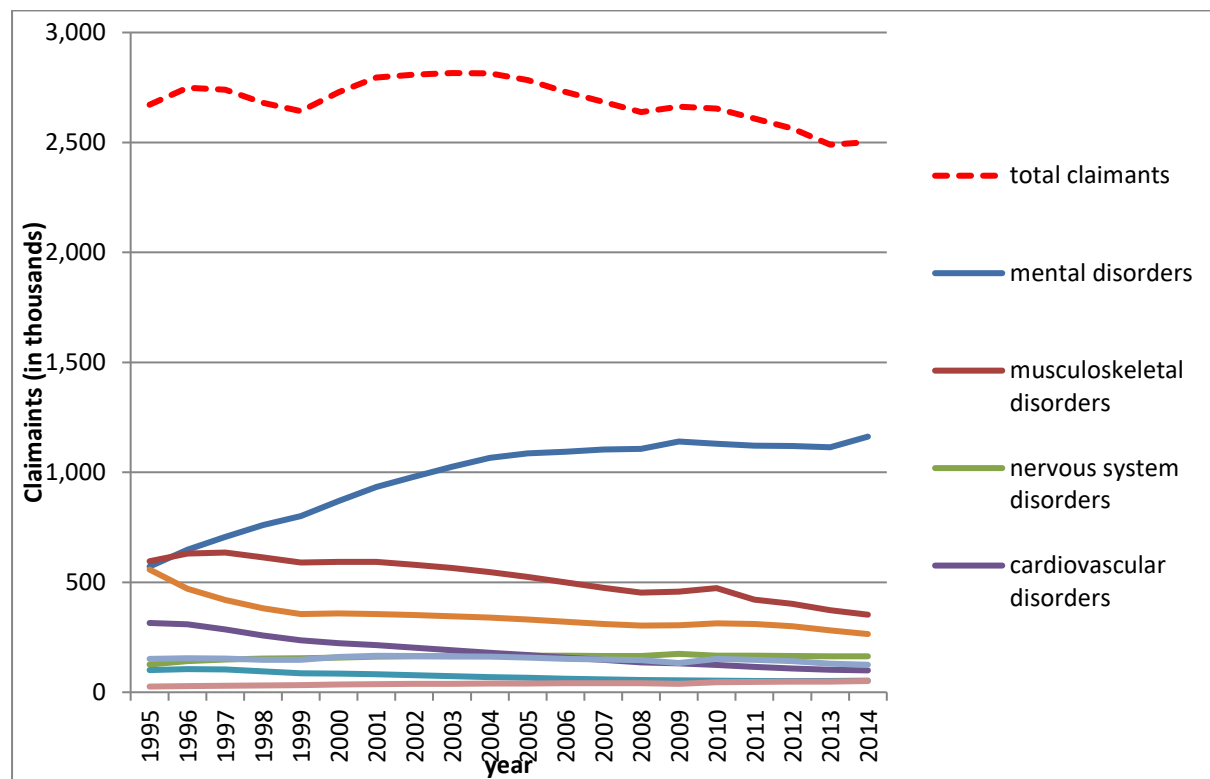
Table 1 Psychoactive effects of psychiatric drugs.

Type of drug	Psychoactive effects*
Antipsychotics	Sedation, subjective and objective cognitive slowing or impairment, emotional blunting/indifference, reduced libido, demotivation, dysphoria (Healy and Farquhar 1998;McClelland et al. 1990;Moncrieff, Cohen, & Mason 2009)
Tricyclic antidepressants	Sedation, cognitive impairment, dysphoria (Dumont et al. 2005;Herrmann and McDonald 1978)
SSRIs and related antidepressants	Drowsiness, lethargy, emotional blunting, loss of libido, 'activation' (agitation, irritability) (Bolling and Kohlenberg 2004;Goldsmith & Moncrieff 2011;Price, Cole, & Goodwin 2009;Safer and Zito 2006)
Lithium	Sedation, cognitive impairment, lethargy, emotional blunting, dysphoria (Judd et al. 1977a; judd et al, 1977b;Muller-Oerlinghausen et al. 1979)
Benzodiazepines	Sedation, cognitive impairment, physical and mental relaxation, euphoria
Stimulants	Increased arousal, vigilance and attention, euphoria.

Table 2

Angels	Demons
Antidepressants	Street drugs
Antipsychotics	Excess alcohol
'Mood stabilisers'	Nicotine
Anti-ADHD drugs	Barbiturates
New anxiolytics (e.g. pregabalin)	Benzodiazepines
Substance misuse treatments	

Figure 1: Trends in claimants of sickness and disability benefits by medical category 1995-2014 (reproduced with kind permission of BJPsych Open, from Viola & Moncrieff, 2016)



References

- Amphetamine advertisement (1940). <https://s-media-cache-ak0.pinimg.com/736x/b8/16/f6/b816f68d76383902a03dd343e72b8fa3.jpg>.
- Balter, M. B., Levine, J., & Manheimer, D. I. (1974). Cross-national study of the extent of anti-anxiety-sedative drug use. *N.Engl.J.Med.*, 290, 769-774.
- Berridge V. (1977) Opium and the historical perspective. *Lancet* Jul 9;2(8028):78-80.
- Bolling, M. Y. & Kohlenberg, R. J. (2004). Reasons for quitting serotonin reuptake inhibitor therapy: paradoxical psychological side effects and patient satisfaction. *Psychother.Psychosom.*, 73, 380-385.
- Boseley, S. and Lignel, B. (2015, November 21). Generation meds: the US children who grow up on prescription drugs. *The Guardian*.
- Boyle, M. (2002). It's all done with smoke and mirrors. Or how to create the illusion of schizophrenia brain disease. *Clinical Psychology*, 12, 9-16.
- Breggin, P. (2008). *Brain-Disabling Treatments in Psychiatry*. (2nd ed.) New York: Springer Publishing Company.
- Breggin, P.R. & Breggin, G.R. (1995) *Talking Back to Prozac*. New York: St Martin's Press
- Busfield, J. (2010). 'A pill for every ill': explaining the expansion in medicine use. *Soc.Sci.Med.*, 70, 934-941.
- Burnham JC. (1968) New perspectives on the Prohibition "experiment" of the 1920's. *Journal of Social History* 2:51-68.
- Ciba (1970). Ritalin advertisement. *Canadian Family Physician*, 16, Back cover.
- Cockburn A, St Claire J. (1998) *Whiteout: The CIA, drugs and the press*. New York: Verso.
- DeGrandpre R. (2006) *The Cult of Pharmacology. How America became the world's most troubled drug culture*. Durham, NC: Duke University Press.
- Dewa, C. S., Hoch, J. S., Lin, E., Paterson, M., & Goering, P. (2003). Pattern of antidepressant use and duration of depression-related absence from work. *Br.J.Psychiatry*, 183, 507-513.
- Dumont, G. J., de Visser, S. J., Cohen, A. F., & van Gerven, J. M. (2005). Biomarkers for the effects of selective serotonin reuptake inhibitors (SSRIs) in healthy subjects. *Br.J.Clin.Pharmacol.*, 59, 495-510.
- Edwards, J. (11-1-2010). AstraZeneca's new Seroquel ad has 5 pages of legal disclaimers. *CBS Moneywatch*. 3-4-2016.

Eli Lilly. (2016). Strattera. <http://www.strattera.com/>. 3-4-2016.

Fava, G. A., Gatti, A., Belaise, C., Guidi, J., & Offidani, E. (2015). Withdrawal Symptoms after Selective Serotonin Reuptake Inhibitor Discontinuation: A Systematic Review. *Psychother.Psychosom.*, 84, 72-81.

Friedan, B. (1963). *The Feminine Mystique*. New York: W.W. Norton.

Gately I. (2008) *Drink: a cultural history of alcohol*. New York: Gotham Books.

Glatt M. (1962) The abuse of barbiturates in the United Kingdom. Bulletin of the United Nations Office on Drugs and Crime 1962. https://www.unodc.org/unodc/en/data-and-analysis/bulletin/bulletin_1962-01-01_2_page004.html

Goldman D. (1966) Critical contrasts in psychopharmacology. In: Rinkel M, editor. *Biological Treatment of Mental Illness*. New York: L.C.Page & Co; p. 524-33.

Goldsmith, L. & Moncrieff, J. (2011). The psychoactive effects of antidepressants and their association with suicidality. *Curr.Drug Saf*, 6, 115-121.

Graham JM.(1972) Amphetamine politics on Capitol Hill. *Society* 9:14-22.

Harrow, M., Jobe, T. H., & Faull, R. N. (2012). Do all schizophrenia patients need antipsychotic treatment continuously throughout their lifetime? A 20-year longitudinal study. *Psychol.Med.*, 1-11.

Healy D. (2006) The latest mania: selling bipolar disorder. *PLoS Med* Apr;3(4):e185.

Healy D. (2004) Shaping the intimate: influences on the experience of everyday nerves. *Soc Stud Sci*, 34:219-245.

Healy, D. & Farquhar, G. (1998). Immediate effects of droperidol. *Hum.Psychopharmacol.*, 13, 113-120.

Herrmann, W. M. & McDonald, R. J. (1978). A multidimensional test approach for the description of the CNS activity of drugs in human pharmacology. *Pharmakopsychiatr.Neuropsychopharmakol.*, 11, 247-265.

Hope, J. (2013). Lazy GPs keep on doling out powerful sleeping pills to the elderly when they should only be used as short-term treatment. *Daily Mail*.

Ilyas S & Moncrieff J. (2012) Trends in prescriptions and costs of drugs for mental disorders in England, 1998 to 2010. *British Journal of Psychiatry* 200:393-398. <http://bjp.rcpsych.org/content/200/5/393.long>

Judd, L. L., Hubbard, B., Janowsky, D. S., Huey, L. Y., & Attewell, P. A. (1977a). The effect of lithium carbonate on affect, mood, and personality of normal subjects. *Arch.Gen.Psychiatry*, 34, 346-351.

Judd, L. L., Hubbard, B., Janowsky, D. S., Huey, L. Y., & Takahashi, K. I. (1977b). The effect of lithium carbonate on the cognitive functions of normal subjects. *Arch.Gen.Psychiatry*, 34, 355-357.

Kiloh LG, Brandon S. (1962) Habituation and addiction to amphetamines. *British medical Journal*, 7;2(5296):40-3.

Kirsch, I., Moore, T. J., Scoboria, A., & Nicholls, S. S. (2002). The emperor's new drugs: an analysis of antidepressant medication data submitted to the US Food and Drug Administration.. *Prevention and Treatment*, 5.

Lader M. (1991) The history of benzodiazepine dependence. *Journal of Substance Abuse Treatment* 8:53-9.

Lewer, D., O'Reilly, C., Mojtabai, R., & Evans-Lacko, S. (2015). Antidepressant use in 27 European countries: associations with sociodemographic, cultural and economic factors. *Br.J.Psychiatry*, 207, 221-226.

Lyapustina, T. & Alexander, G. C. (2015). the prescription opioid addiction and abuse epidemic: how it happened and what we can do about it. *The Pharmaceutical Journal*, 2015.

McClelland, G. R., Cooper, S. M., & Pilgrim, A. J. (1990). A comparison of the central nervous system effects of haloperidol, chlorpromazine and sulpiride in normal volunteers. *Br.J.Clin.Pharmacol.*, 30, 795-803.

Moncrieff, J. (2008a). *The Myth of the Chemical Cure: a critique of psychiatric drug treatment*. Basingstoke, Hampshire, UK: Palgrave Macmillan.

Moncrieff, J. (2008b). The creation of the concept of the antidepressant: an historical analysis. *Social Science and Medicine*, 66, 2346-2355.

Moncrieff, J., Cohen, D., & Mason, J. P. (2009). The subjective experience of taking antipsychotic medication: a content analysis of Internet data. *Acta Psychiatr.Scand.*, 120, 102-111.

Moncrieff, J. (2009). A critique of the dopamine hypothesis of schizophrenia and psychosis. *Harv.Rev.Psychiatry*, 17, 214-225.

Moncrieff, J. (2011). From neuroleptics to antipsychotics: the emergence of ideas of disease-specificity in relation to early antipsychotics. *in preparation*.

Moncrieff J, Cohen D & Porter S.(2013) The psychoactive effects of psychiatric medications: the elephant in the room. *Journal of Psychoactive Drugs*, 45:409-415.

Moncrieff, J. (2013). Magic bullets for mental disorders: the emergence of the concept of an "antipsychotic" drug. *J.Hist Neurosci.*, 22, 30-46.

Moncrieff, J. (2014). The Chemical Imbalance Theory of Depression: still promoted but still unfounded. <http://joannamoncrieff.com/2014/05/01/the-chemical-imbalance-theory-of-depression-still-promoted-but-still-unfounded/> [On-line]. Available: <http://joannamoncrieff.com/2014/05/01/the-chemical-imbalance-theory-of-depression-still-promoted-but-still-unfounded/>

Moncrieff, J. & Kirsch, I. (2015). Empirically derived criteria cast doubt on the clinical significance of antidepressant-placebo differences. *Contemp.Clin.Trials*, 43, 60-62.

Muller-Oerlinghausen, B., Hamann, S., Herrmann, W. M., & Kropf, D. (1979). Effects of lithium on vigilance, psychomotoric performance and mood. *Pharmakopsychiatr.Neuropsychopharmakol.*, 12, 388-396.

Pratt, L. A., Brody, D. J., & Gu, Q. (2011). *Antidepressant use in persons aged 12 and over: United States 2005-2008. NCHS data brief no 76*. Hyattsville, MD: National Center for Health Statistics.

Prescribing and Medicines Team: Health and Social Care Information Centre (2015). *Prescriptions dispensed in the community. England 2004-2014*. London: Health and Social Care Information Centre.

Price, J., Cole, V., & Goodwin, G. M. (2009). Emotional side-effects of selective serotonin reuptake inhibitors: qualitative study. *Br.J.Psychiatry*, 195, 211-217.

Public Health England (2014). Advice for prescribers on the risk of the misuse of pregabalin and gabapentin.

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385791/PHE-NHS_England_pregabalin_and_gabapentin_advice_Dec_2014.pdf [On-line]. Available: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385791/PHE-NHS_England_pregabalin_and_gabapentin_advice_Dec_2014.pdf

Rasmussen N. (2006) Making the first antidepressant; Amphetamine in American medicine 1929-1950. *Journal of the History of Medicine and Allied Sciences* 61(3):288-323.

Rasmussen N. (2008) America's first amphetamine epidemic 1929-1971: a quantitative and qualitative retrospective with implications for the present. *Am J Public Health* 98(6):974-85.

Safer, D. J. & Zito, J. M. (2006). Treatment-emergent adverse events from selective serotonin reuptake inhibitors by age group: children versus adolescents. *J.Child Adolesc.Psychopharmacol.*, 16, 159-169.

Salvo, F., Pariente, A., Shakir, S., Robinson, P., Arnaud, M., Thomas, S. et al. (2016). Sudden cardiac and sudden unexpected death related to antipsychotics: A meta-analysis of observational studies. *Clin.Pharmacol.Ther.*, 99, 306-314.

Wallace Laboratories (1967). Miltown advertisement. *JAMA*, 202, 54-56.

Wallace Laboratories (1964). Miltown advertisement.

<http://prescriptiondrugs.procon.org/view.resource.php?resourceID=005687>.

Wallace Laboratories (undated). Miltown advertisement. <http://homeeverafter.com/wp-content/uploads/2010/05/MiltownPregnantHomemaker.jpg>

Wikipedia (2015) Vin Mariani. https://en.wikipedia.org/wiki/Vin_Mariani

Wunderink, L., Nieboer, R. M., Wiersma, D., Sytema, S., & Nienhuis, F. J. (2013). Recovery in Remitted First-Episode Psychosis at 7 Years of Follow-up of an Early Dose Reduction/Discontinuation or Maintenance Treatment Strategy: Long-term Follow-up of a 2-Year Randomized Clinical Trial. *JAMA Psychiatry*.

Wyeth Laboratories (1967). Serax advertisement. *JAMA*, 200, 206-207.